Functional Properties of Human Primary Motor Cortex Gamma Oscillations

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Muthukumaraswamy SD. Functional properties of human primary motor cortex gamma oscillations. J Neurophysiol 104: 2873–2885, 2010. First published September 8, 2010; doi:10.1152/jn.00607.2010. Gamma oscillations in human primary motor cortex (M1) have been described in human electrocorticographic and noninvasive magnetoencephalograhic (MEG)/electroencephalographic recordings, yet their functional significance within the sensorimotor system remains unknown. In a set of four MEG experiments described here a number of properties of these oscillations are elucidated. First, gamma oscillations were reliably localized by MEG in M1 and reached peak amplitude 137 ms after electromyographic onset and were not affected by whether movements were cued or self-paced. Gamma oscillations were found to be stronger for larger movements but were absent during the sustained part of isometric movements, with no finger movement or muscle shortening. During repetitive movement sequences gamma oscillations were greater for the first movement of a sequence. Finally, gamma oscillations were absent during passive shortening of the finger compared with active contractions sharing similar kinematic properties demonstrating that M1 oscillations are not simply related to somatosensory feedback. This combined pattern of results is consistent with gamma oscillations playing a role in a relatively late stage of motor control, encoding information related to limb movement rather than to muscle contraction.

INTRODUCTION

The widespread presence and modulation of band-limited neuronal oscillations within the brain suggest they constitute a fundamental mechanism used for information processing. One such oscillation, the gamma oscillation (~30–100 Hz), has been proposed as a temporal coding scheme by which distributed neuronal groups are synchronized, enabling the transmission of information (Engel and Singer 2001; Engel et al. 2001; Fries et al. 2007). Indeed, gamma oscillations have been described in a variety of sensory (Gray et al. 1989), perceptual (Tallon-Baudry and Bertrand 1999), and memory systems (Jensen et al. 2007). Gamma oscillations in human motor cortex were first described in electrocorticographic (eCoG) recordings by Crone et al. (1998), with subsequent confirmation by a number of other invasive investigations (Miller et al. 2007; Nagasawa et al. 2010; Pfurtscheller et al. 2003; Szurhaj et al. 2005, 2006). The results of these studies are generally in agreement that gamma oscillations in motor cortex occur in a frequency range of 60–100 Hz, are evoked primarily contralateral to the moving body part, are more somatotopically organized than lower-frequency alpha and beta rhythms, and are most prevalent during movement onset. Several groups have now demonstrated that noninvasive techniques (electroencephalography/magnetoencephalography [EEG/MEG]) give patterns of results very similar to those of invasive recordings (Cheyne et al. 2008; Donner et al. 2009; Gaetz et al. 2010; Huo et al. 2010; Tecchio et al. 2008; Waldert et al. 2008) and the validity of using noninvasive approaches to study motor cortex gamma oscillations has been confirmed by direct comparisons of invasive and surface EEG (Ball et al. 2008; Darvas et al. 2009).

Although noninvasive techniques can therefore be used to probe the function of motor cortex gamma oscillations, in the neocortex, gamma oscillations have been most thoroughly experimentally described in the visual system. Numerous experimental studies have attempted to elucidate the function of visual gamma oscillations by systematically varying stimuli across dimensions, such as stimulus contrast (Hall et al. 2005), spatial frequency (Adjamian et al. 2004; Muthukumaraswamy and Singh 2008, 2009), and motion (Siegel et al. 2007; Svetkenham et al. 2009). However, analogous studies systematically addressing the effects of movement parameters on the motor cortex do not exist and the functional role of motor cortex gamma oscillations in motor control is unknown. The four studies in this work each systematically probe a different aspect of motor cortex gamma oscillation activity in relation to motor behavior using MEG. In experiment 1 participants performed index finger abductions either cued by an auditory tone or self-paced with and without a displacement meter present. To examine the effects of movement frequency and magnitude in experiment 2 participants performed index finger abductions of two magnitudes at three frequencies. To investigate static force production in experiment 3 participants performed near-isometric contraction of the index finger at two force levels. Finally, the role of motor commands versus sensory feedback in the generation of motor cortex gamma oscillations was examined in experiment 4 by comparing active movements performed by the participant with passive movements in which participants’ fingers were moved for them by an experimenter.

METHODS

Participants

Nineteen healthy volunteers took part in the four experiments after giving informed consent, with all procedures approved by the local ethics committee. Table 1 provides details of the sex and age of each participant as well as which experiments they took part in. All participants previously volunteered for experiments in CUBRIC (Cardiff University Brain Research Imaging Centre) and had anatomical magnetic resonance imaging (MRI) scans (1 mm isotropic prepared fast spoiled gradient recalled echoes) available for analysis.

Experimental paradigms

Experiment 1. In this experiment participants performed ballistic abductions of the right-hand index finger in three blocked conditions: cued, self-paced, and self-paced with no displacement meter. In the
cued condition abductions were performed to an auditory pip played through insert headphones (3.5–4.5 s interpip interval). In the self-paced condition participants were instructed to perform the movements to the same rhythm as that for the cued condition. If the intermovement interval became too large or small the experimenter instructed them by intercom to moderate their speed appropriately. In both the cued and self-paced conditions participants’ index fingers were lightly attached to a piece of plastic (see Data acquisition) to measure displacement. The maximum allowable finger displacement was 15 mm. The self-paced with no displacement meter condition was identical to the self-paced condition but the displacement-measuring apparatus was removed from the MEG-shielded room. Each condition continued for 20 min, with conditions performed in a fixed order. This resulted in about 275 flexions per condition. In all experiments participants passively fixated on a spot on the wall in front of them. The self-paced condition was nearly identical to the MEG paradigm used in Cheyne (2008), with increased trials/time intended to replicate these results. The cued condition was included to test whether cueing abductions would also reliably elicit gamma-band activity. Finally, the no displacement meter condition was included to check for possible effects/interference of the movement-measuring device on gamma-band oscillatory activity.

**Experiment 2.** In experiment 2 participants performed repetitive abductions of the right index finger against the displacement meter in blocks of 4 s followed by 4.5 s of rest. Abductions were performed to auditory pips played at either 1 Hz (4 abductions), 2 Hz (8 abductions), and 3 Hz (12 abductions), each at two movement depths (~4 and ~8 mm), creating 6 conditions in a 2 × 3 factorial design. Each condition was separated into blocks of 65 trials that lasted for a total of about 10 min, with the order of conditions randomized across participants. Prior to performing each condition participants received several minutes of feedback training, during which they could monitor their performance using a real-time visual display that showed the continuous displacement signal of the force meter output. Each condition consisted of 100 trials with the order of conditions randomized.

**Experiment 4.** Experiment 4 consisted of participants performing large movements at 2 Hz exactly as in experiment 2, here termed the active movement condition. In a second passive movement condition an experimenter sat in the MEG-shielded room to the side of participants located out of their field of view. The experimenter (SDM) used the same auditory pips to passively move the plastic attached to the displacement-measuring device (see following text), thus moving participants’ fingers with approximately the same motion as that in the active movement condition. Participants were unable to hear the tone pips in the passive movement condition. For the passive movement condition participants received several minutes of training in which they learned to relax their fingers during passive movement by watching their running electromyographic (EMG) trace. In all, 65 trials were run in each block, although participants P16 and P17 performed 100 trials of each. The passive movement condition was always performed second.

**Data acquisition**

All MEG recordings were made using a whole head CTF-Omega 275-channel radial gradiometer system sampled at 1,200 Hz (0–300 Hz band-pass). An additional 29 reference channels were recorded for noise cancellation purposes and the primary sensors were analyzed as synthetic third-order gradiometers (Vrba and Robinson 2001). Three of the 275 channels were turned off due to excessive sensor noise. Participants were fitted with three electromagnetic head coils (nasion and preauriculars), which were localized relative to the MEG system immediately before and after the recording session. Simultaneous EMG recordings were made from participants’ right FDI and digitized with the MEG data. In experiments 1, 2, and 4 participants’ fingers were lightly attached to a small piece of plastic, attached to an optical displacement system. This device gave a one-dimensional measure of displacement (in the direction of FDI abduction), which was continuous and preauriculars). In all, 65 trials were run in each block, although participants P16 and P17 performed 100 trials of each. The passive movement condition was always performed second.

**Supplemental Table 1. Participant sex and age demographics with the experiments each took part in indicated**

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8 F/11 M Mean = 25.1 n = 6 n = 10 n = 8 n = 7

The online version of this article contains supplemental data.
duced and this was simultaneously sampled with the EMG. The voltage–force function of this device is displayed in Supplemental Fig. S1R. Additional vertical and horizontal electrooculograms were recorded in experiments 1, 2, and 3.

Data analysis

General procedures. Epoched MEG data were first visually inspected and trials contaminated with large artifacts, such as head movements or large muscle artifacts were removed from the analysis. Source localization was then performed on the MEG data using the SAM (synthetic aperture magnetometry) beamformer (Robinson and Vrba 1999). To achieve MRI/MEG coregistration, prior to the MEG acquisition, fiduciary markers were placed at fixed distances from anatomical landmarks identifiable in participants’ anatomical MRIs (tragus, eye center). Fiduciary locations were verified afterward using high-resolution digital photographs. For source localization a multiple local-spheres (Huang et al. 1999) forward model was derived by fitting spheres to the brain surface extracted by the Oxford FMRI Software Library Brain Extraction Tool (FSL BET; Smith 2002). Each data set was then band-pass filtered into three frequency bands: 60–90, 30–60, and 15–40 Hz. The choice of 60–90 Hz to analyze gamma—the focus of this work—was derived from previous research investigating motor cortex gamma oscillations using MEG (Cheyne et al. 2008). The SAM algorithm was then used to create differential images of source power (pseudo T statistics) for baseline versus active conditions for each of the frequency bands. Details of the calculation of SAM pseudo T source image statistics are described in detail in a number of sources (Cheyne et al. 2003; Hillebrand et al. 2005; Robinson and Vrba 1999; Singh et al. 2003). Estimates of the three-dimensional distribution of source power were derived for the entire brain at 4 mm isotropic voxel resolution. After generating dual-state SAM images the peak location of gamma-band (60–90 Hz) activity in the contralateral primary motor cortex (M1) was identified in the gamma-band image and subjected to further analysis. Specifically, virtual sensors were generated from these peak motor cortex locations using SAM beamformer coefficients generated using covariance matrices derived from the band-pass (60–90 Hz) filtered MEG data. To reveal both induced and evoked responses, time–frequency analysis of virtual sensors was conducted using the Hilbert transform between 1 and 100 Hz at 0.5-Hz frequency step intervals, filtering with an 8-Hz wide-band, third-order Butterworth filter (Le Van Quyen et al. 2001).

All EMG data were analyzed by first band-pass filtering from 15 to 300 Hz with a 50-Hz notch filter and then rectifying (Cheyne et al. 2008).

Analysis details: experiment 1. From the continuous MEG recordings in this experiment, EMG onsets were marked using an automated algorithm that marked increases in the rectified EMG signal by 3SDs above the noise floor (Cheyne et al. 2008). Once a marker was placed the next marker could only be placed a minimum of 2 s later. False positives were detected visually and discarded from analysis. All data were then epoched from 1.5 s before to 1 s after the EMG markers. This approach allowed all three conditions in experiment 1 to be analyzed with the same event (EMG onset) at time = 0 s. Following the optimal parameters determined by Cheyne et al. (2008), SAM source localization analysis was conducted using an active window of 0–0.3 s and a passive window of ~1.3 to 1 s. This choice of optimal time–frequency bands was verified by inspection of the current data (see time–frequency analyses in Figs. 1 and 2). In this experiment individual gamma-band source power images were statistically thresholded using a permutation-based method. In this approach, the labeling of active and control data was randomly permuted and new covariance matrices and SAM images were generated for the permuted data (Cheyne et al. 2003). Each SAM image was recomputed 1,000 times. To statistically threshold and correct for multiple comparisons, the omnibus test statistic obtained from the permutation distribution (Nichols and Holmes 2002) was used ($P < 0.05$). Time–frequency plots for this experiment were baselined from −1.5 to −0.5 s and Student’s $t$-statistics and associated $P$ value (two-sample $t$-test) spectrograms calculated using the single-trial time–frequency estimates for each pixel in the time–frequency spectrogram. A longer baseline period could be used for the time–frequency analysis (more stable) compared with the SAM source analysis, which requires that baseline and active covariance matrices be equally matched with respect to the number of samples used (Robinson and Vrba 1999). To correct for multiple comparisons in time–frequency analysis the false discovery rate (FDR) was controlled (Benjamini and Hochberg 1995) and applied as a threshold on the time–frequency spectrograms. To compare between all three conditions in a single analysis a similar approach was used, instead using $F$-statistics, and where pairwise contrasts were required, independent-samples $t$-tests were performed.

Analysis details: experiments 2 and 3. For these experiments SAM analyses were conducted using an active window of 0–4 s (where 0 = auditory cue onset) and a passive period of −4 to 0 s. Time–frequency plots were baselined from −4 to −1 s. Thresholding for individual spectrograms used an approach similar to that of experiment 1 and for group time–frequency analysis, $t$-statistics were calculated across participants instead of trials. In experiment 2 statistical analysis percentage change spectrograms were generated and gamma-band activity was integrated between 0 and 4 s and 60 and 90 Hz. Two-way repeated-measures ANOVA was then performed on these data.

Analysis details: experiment 4. The data for the active movement condition were analyzed exactly in accord with the similar (2 Hz large) condition in experiment 2. For the passive movement condition similar SAM images were generated, although some participants had little or no gamma-band power increases in the source images. For these participants virtual sensor locations were based on the peak source power decreases in the beta-band images in contralateral motor cortex. This approach was reasonable, based on both the data collected in the experiments here and previous work, where beta power decrease and gamma power increases are closely co-located (Gaetz et al. 2010). Further, for images with low source power, the spatial full width at half-maximum (FWHM) of the beamformer becomes wider (Barnes and Hillebrand 2003), thus ameliorating any negative effects of this procedure. Virtual sensors were then constructed from these peak locations as in the active movement condition. Trials in which any sample of the rectified EMG showed activity $>0.1$ mV were discarded from the analysis. Participant P15 showed EMG activity on almost every “passive movement” trial and thus his data were excluded from the analysis. The other participants had rejection counts of between 0 and 16 trials. Trials were discarded after generating the beamformer coefficients such that each beamformer weight vector was generated from approximately evenly sized data sets. For each condition single-trial gamma-band amplitude estimates were obtained by integration of the single-trial time–frequency estimates (0–4 s; 60–90 Hz). These data were subjected to one-sample $t$-test to test for the presence of significant gamma activity in each condition and independent-sample $t$-test to compare conditions in each participant.

Results

Experiment 1

Figure 1 illustrates data from a single participant, i.e., data that characterize the data analysis workflow and typical results from experiment 1. In Fig. 1, A and B, a clear onset of EMG activity occurs at time 0, although there is a small buildup of the average rectified EMG signal in the 200 ms preceding time 0. The movement itself peaked around 150 ms, with the finger returning to its resting position within 500 ms from EMG onset. In Fig. 1C example sensor-level integrated gamma-band activity is presented (60–90 Hz; 0–0.3 s). Importantly, the
spatial distribution demonstrates two peak increases in power (red) consistent with a left hemisphere source somewhere near the central sulcus when measured with axial gradiometers. Moreover, there is little activity elsewhere in the topography, for example, near the eyes, indicating little contamination in this frequency band with eye or other physiological artifacts. In Fig. 1 the time–frequency reconstruction of a single MEG sensor, at which sensor-level gamma-band activity is maximal, is presented. All subsequent MEG analyses herein are derived from estimated source-level activity. In Fig. 2, reconstructed gamma-band activity for the cued condition is presented for all six participants in experiment 1 and plotted on partially inflated cortical mesh models generated from each participant’s MRI. Significant gamma-band activity was reconstructed in all six participants in all conditions. Table 2 provides the locations of the peak location of gamma-band activity for each participant and condition following spatial normalization to the average Montreal Neurological Institute brain. The majority of peak locations and the grand mean peak location were in the contralateral M1. Supplemental Fig. S2 illustrates that gamma-band activity was significant for all conditions and participants, with functional images overlaid onto axial T1 images from each participant. These images demonstrate that gamma-band activity was predominantly located anterior to the central sulcus near the motor cortex hand “knob.”

Although significant gamma-band activity was present for all participants and conditions there was considerable variability in response amplitude across participants. This was evident in both the source localization images (peak pseudo T range: 3.0–13.5) and also in the time–frequency spectrograms in Fig. 2, where the Student’s t-statistics range from 6 to 15. The peak frequency range for the six participants showed a relatively small range of 73.5–81 Hz (mean 78.2 Hz). Across the 18 runs the grand-average time to peak time of gamma-band activity was 137 ms after EMG onset (SD = 51 ms; max = 262 ms; min = 66 ms). To investigate the phase-locking characteristics of gamma-band activity the phase-locking values (Tallon-Baudry et al. 1997) associated with the virtual sensor plots were calculated, as well performing averaging in the time domain. Although all data displayed previously described movement-related fields (Cheyne et al. 2008), the phase-locking value plots (Supplemental Fig. S3) and time–frequency analysis of the movement-related fields (Supplemental Fig. S4) did not demonstrate any systematic activity in the time–frequency range of the induced activity. Thus a reasonable conclusion from this is the gamma-band activity reported here is not phase-locked (induced) relative to the onset of EMG activity and is not a “ripple” overlaid on the movement-evoked fields (or that the EMG onset marking procedure is not temporally precise enough to determine such high-frequency phase-locking).

Figure 3 plots the grand-averaged integrated gamma-band (60–90 Hz) activity data (% change) for the time range 0–0.3 s. A nonparametric Friedman ANOVA did not detect any differences between the three conditions (P = 0.6). Furthermore, F-statistic spectrograms and corresponding P value im-
The gamma-band power was calculated for each participant for the three conditions. The uncorrected and corrected P value images are presented in Supplemental Fig. S5. Neither these images nor post hoc independent-samples t-test spectrograms indicated any trend for gamma-band activity to be systematically different between the three conditions.

**Experiment 2**

Figure 4A displays the behavioral and EMG measures for experiment 2 examining the effects of movement depth and movement frequency. Clear peaks are present in both the EMG and displacement traces for each movement and the "peaky" rather than sinusoidal nature of the trace indicates participants were making ballistic rather than smooth sinusoidal movements as instructed. The movement data were quantified into two variables: mean peak-to-peak displacement and total displacement. The first measure (Fig. 4B) provides an index of the movement depth of individual movements and the second measure (Fig. 4C), the total amount of movement performed per trial. A repeated-measures ANOVA on the peak-to-peak displacement data demonstrated a main effect of size [$F_{(1,9)} = 68.267, P < 0.001$] and a smaller main effect of frequency [$F_{(2,18)} = 5.67, P < 0.02$], but no interaction effect [$F_{(2,18)} = 0.14, P = 0.86$]. A repeated-measures ANOVA on the total positive displacement data demonstrated significant main effects of size [$F_{(1,9)} = 60.91, P < 0.001$] and frequency [$F_{(2,18)} = 58.95, P < 0.001$] and also an interaction effect [$F_{(2,18)} = 15.79, P < 0.001$].

Figure 5 demonstrates time–frequency spectrograms for a single participant (P3) for each condition and these demonstrate rich response morphology from M1. For the gamma band, a distinct burst of gamma power increases can be seen at each movement, although at 3-Hz movement frequency these tend to become temporally blurred. Beta (≈15–40 Hz) power decreases are present in all conditions and in the 1-Hz conditions are interspersed with rebound power increases. Low-frequency components corresponding to the motor-evoked field can be seen with each movement. Figure 6 displays similar time–frequency spectrograms for grand-averaged statistical data and similar patterns are present. The plots in Fig. 6 suggest that gamma-band activity was not sustained for the smaller movements, although inspection of the unthresholded time–frequency statistical plots (Supplemental Fig. S6) indicates the presence of weak sustained gamma activity. A repeated-measures ANOVA on the integrated gamma-band data
(Fig. 7) demonstrated a linear main effect of movement size on gamma-band power increases for each condition and participant in experiment 1, corresponding closest Brodmann Area of the peak of gamma-band activity was higher for the first movement in a sequence over subsequent movements (others n.s.).

For the 1 Hz large condition ANOVA showed a significant effect of movement sequence number on gamma-band power (F = 5.508, P < 0.004), with post hoc comparisons showing that movement 1 was higher in frequency than movements 2 (t = 5.123, P < 0.002), and 4 (t = 2.768, P < 0.03; others n.s.). For the 1 Hz small condition ANOVA showed a significant effect of movement sequence number on gamma-band power (F = 5.616, P < 0.004). Post hoc analysis showed that movement 1 had the highest frequency (1 vs. 2, t = 4.9, P < 0.001; 1 vs. 3, t = 4.66, P < 0.001; 1 vs. 4, t = 2.33, P < 0.045; others n.s.). For the 2 Hz large condition ANOVA showed no effect on gamma-band frequency (F = 0.0847, n.s.). For the 2 Hz small condition ANOVA showed a main effect of movement sequence number on gamma-band frequency (F = 4.25, P < 0.001), with post hoc comparisons showing movement 1 to be higher than movements 3 through 7 and movement 2 to be >5, 6, and 7. To summarize, these results indicate that the first movement in a repetitive movement sequence has the largest gamma-band power. Although slightly less definitive, the data also indicated that the first movement of a sequence was higher in frequency compared with that of subsequent movements. To test whether this result was possibly influenced by better time-locking of the first movement in a sequence, a similar analysis was conducted by resynchronizing each movement in the sequence to the EMG onset of that movement. The details and results of this analysis are contained in the Supplemental data, with the results showing the pattern of results was identical to that introduced earlier.

Experiment 3

Figure 8A plots the data from a single participant (P3) from experiment 3, where participants were asked to maintain static

![Gamma Band Change](http://jn.physiology.org/)

**FIG. 3.** Grand-averaged integrated gamma-band source activity derived from time–frequency spectrograms for the cued, self-paced, and no displacement meter condition, respectively, for experiment 1.
force with near-isometric contraction against a rigid air-pressure tube and Fig. 8B plots the equivalent group-level data. The behavioral plots of both figures (top left) demonstrate a clear gradation in terms of the magnitude of force production between the two conditions and that, during the experiment, participants were able to maintain the set force level very accurately. The extra motor requirements of producing this extra force are mirrored in the rectified EMG activity (Fig. 8A and B, top right plots), where clearly more EMG is evident in the large force condition. Although the EMG activity showed a peak of activity near the onset of force production graded EMG activity is clearly maintained for the onset of force production. Time–frequency spectrograms (Fig. 8A and B, bottom panels) show evidence of components similar to those of experiment 2, with the presence of gamma power increase, beta power decrease, and a low-frequency onset response. Interestingly, strong gamma-band activity was present only at the onset of force production and not during the maintenance of static contraction, as evidenced by the time–frequency spectrograms. However, beta power source decreases were maintained for the entire duration of force production. Although pixelwise independent-samples t-test did not reveal significant gamma effects between conditions when gamma was integrated between 60 and 90 Hz over a time range of 0.2–0.7 s, gamma power was found to be significantly greater in the large force condition \( t_{(8)} = 3.16, P < 0.02 \). One-sample t-test on the integrated gamma also found significant gamma power in both conditions [large force \( t_{(8)} = 6.08, P < 0.001 \); small force \( t_{(8)} = 5.49, P < 0.001 \)]. No difference was found between beta (15–40 Hz) power decreases between the two conditions \( t_{(8)} = -1.64, P = 0.13 \), consistent with previous reports (Andrykiewicz et al. 2007).

As a further control for the use of auditory stimulation to cue movements, in a separate recording session two participants (P3 and P9) were subjected to auditory stimulation with all experimental apparatus present but no movement requirements. No gamma-band power increases were seen (see Supplemental Fig. S7).

**Experiment 4**

Figure 9A plots group-averaged data from experiment 4, which examined the effects of passive versus active movements on M1. Figure 9A (top left) shows the finger movement traces from the two conditions and it can be seen that the experimenter was attempting to “imitate” the active movements. The passive movements had a tendency to lag slightly behind the active movements temporally and went through a slightly larger range of motion; as such, both peak-to-peak displacement and total displacement (cf. experiment 2, Fig. 4) of the finger were actually larger in the passive movement condition than in the active condition. Figure 9A (top right) shows that EMG activity in the...
active movement condition was very similar to the condition in experiment 2 and as expected, due to removal of trials with EMG activity, the passive movement condition showed no EMG activity. Unthresholded time–frequency spectrograms for the two conditions are presented in Fig. 9A (bottom panels) and the gamma activity is strikingly different between the two conditions. Although gamma activity can be seen at each movement peak in the active movement condition it is largely absent in the passive movement condition apart from a very small amount at the initial onset of movement. Beta power decreases and low-frequency power increases are present in both conditions, although the beta event-related desynchronization is reduced in the passive movement condition. To statistically analyze the gamma-band effects, single-trial gamma-band source amplitude estimates were obtained for each participant and trial, with the results plotted in Fig. 9B. Gamma-band activity was clearly significant in all participants for the active movement condition but was clearly reduced in the passive movement condition and only significantly in four participants. In fact, P16 showed significant negative gamma amplitude changes. Use of a t-test (Fig. 9B) demonstrated that gamma amplitude was clearly significantly different in five of the participants, with the one participant reaching marginal significance ($P = 0.055$). Grand-averaged gamma-band amplitude in the active movement condition was 0.22 and 0.005 nAm in the passive movement condition (44-fold greater).

**DISCUSSION**

In this study gamma oscillations were systemically investigated using task manipulations designed to begin to elucidate the functional role of these oscillations in motor control. In experiment 1, the self-paced abduction condition was almost identical to that used in previous MEG investigations, with a very similar pattern of results obtained (Cheyne et al. 2008). However, the critical addition to this previous work was to directly compare gamma oscillations between internally generated (self-paced) and externally directed (cued) conditions—a manipulation performed for both pragmatic and theoretical reasons. Pragmatically speaking, being able to externally cue participants to move, such as with the auditory tone used here, allows more sophisticated movement paradigms to be generated (as in experiments 2–4) and also leads to tighter control of the experimental paradigm in terms of timing. This experiment, as well the control recordings for experiment 3 (Supplemental Fig. S7), confirmed that auditory stimuli do not cause artifactual gamma-band responses in M1 or affect the basic form of the gamma-band response. The theoretical reason

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**FIG. 5.** Thresholded ($P < 0.05$, corrected) time–frequency spectrograms for each condition in experiment 2 for a single participant (P3) obtained from virtual sensors placed in the primary motor cortex (M1). The dependent variable is Student’s $t$-statistic. Time 0 = tone onset.
for this manipulation was that there exists considerable evidence from both monkeys and humans for selective recruitment of elements of the motor system under these differing experimental requirements. Functional brain imaging studies have found that internally generated movements preferentially activate the supplementary motor area (SMA), whereas externally directed actions preferentially activate the lateral premotor cortex (Deiber et al. 1991, 1996). EEG measures have also shown that the duration of activity in SMA is longer for internally generated actions and longer in lateral premotor cortex for externally directed actions (Thut et al. 2000). Although gamma oscillations are generated in M1 (Cheyne et al. 2008; Miller et al. 2007) (at a lower schematic level in the motor system), it was important to validate that similar patterns of activity would be obtained from the two conditions. The final pragmatic goal achieved by experiment 1 was to validate the use of the displacement-measurement device because it was not clear a priori whether attaching the finger to the small piece of plastic and very slight resistance would affect the gamma oscillations, especially if gamma oscillations were to be modulated by discriminative touch systems. However, no evidence for this was found and experiment 4 suggests that the gamma oscillations reported here are not generated by discriminative touch systems.

Exploratory analyses in both sensor and source space as well as those presented here (Fig. 2; Supplemental Fig. S6) suggested that the only consistent source of gamma-band oscillations in these relatively simple behavioral paradigms when recording with MEG are from contralateral M1. Although the beamformer source localization images may appear relatively dif-
fuse, it is important to note that adjacent beamformer voxels are highly spatially correlated with weaker sources tending to have larger FWHMs (Barnes and Hillebrand 2003). Human eCoG work has demonstrated that gamma-band responses display distinct homuncular organization such that individual digits can be spatially separated with the use of appropriate analytic techniques (Miller et al. 2009). In the present data there was little evidence for high-frequency activity occurring in higher-level motor control areas such as the supplementary or premotor cortices and therefore little a posteriori reason to attempt to parcellate function between these structures or to attempt connectivity analyses such as coherence analysis. By contrast in electrocorticographic studies have been reported in some subjects gamma oscillations in premotor (Brovelli et al. 2005) and supplementary motor areas (Szurhaj et al. 2005). This difference may be caused by a number of factors including: 1) the relatively simple behavioral tasks used here (Brovelli et al. 2005), 2) the lack of sensitivity of MEG to recording radially oriented sources, 3) possible source cancellation effects across the central fissure for SMA (Lang et al. 1991), and 4) the relatively lower signal to noise ratio of MEG. Some higher-order motor areas may not necessarily exhibit the required spatial summation of gamma activity to generate reliable MEG signals (it should be noted that the amplitude of gamma oscillations here is ~10 fT, which is just above the noise floor for the MEG detectors used). That said, for M1, the current data clearly demonstrate that statistically significant, spatially reproducible gamma oscillations can be recorded from the M1 in healthy human volunteers and, as such, MEG can be used as a tool for investigating the functional role of this specific set of oscillations in human motor control. This is an important point because eCoG studies are restricted to patients with intractable epilepsy with lengthy medication histories.

The results of the current work strongly indicate that the source of the oscillations under consideration here are located anterior of the central sulcus in the M1 (see Table 1), rather than in the somatosensory cortex, and this is consistent with previous MEG studies using similar paradigms and analytic methodologies (Cheyne et al. 2008; Gaetz et al. 2010). Gamma-band oscillations have been previously described in MEG recordings with the use of both median nerve stimulation (Fukuda et al. 2010; Gaetz and Cheyne 2003; Hagiwara et al. 2010) and more.

FIG. 8. A: data from a single participant (P3) from experiment 3 examining the effects of differential force production in M1. The top left plot displays the mean force produced across trials, with the shading representing the SE. The top right plot is similar but instead rectified EMG activity is plotted. The bottom left plot represents the time–frequency spectrum from the large force condition and the bottom right plot from the small force condition. Units for spectrograms are Student’s t-statistics (threshold $P < 0.05$, corrected). B: group data from experiment 3 examining the effects of differential force production in M1. The top left plot displays the mean force produced across trials, with the shading representing the SE. The top right plot is similar but instead rectified EMG activity is plotted. The bottom left plot represents the time–frequency spectrum from the large force condition and the bottom right plot from the small force condition. Units for spectrograms are Student’s t-statistics (threshold $P < 0.05$, corrected). Time 0 = tone onset.
naturalistic stimulation techniques (Bauer et al. 2006) in the postcentral gyrus, indicating somatosensory cortex is also capable of producing macroscopic gamma-band oscillations. However, the lack of gamma-band activity in the passive movement condition of experiment 4 would argue against the fact that the gamma-band oscillations recorded here are a somatosensory phenomenon. Gamma-band oscillations may still be occurring in somatosensory cortex during the paradigms used here that techniques with higher spatial resolution such as local field potential or eCoG recordings might be able to detect. However, the gamma-band activity in the present work is best interpreted as being located in the M1 and being reflective of active motor processes.

Consistent with previous studies (Cheyne et al. 2008; Gaetz et al. 2010; Szurhaj et al. 2006) these results demonstrate that the bulk of gamma oscillation activity occurs at or after EMG onset. Although small amounts do occur slightly before EMG onset (Miller et al. 2009), this may be due to the conservative nature of the EMG marking process, because one can see some slight buildup in the averaged rectified EMG activity prior to time = 0 s (Fig. 1). This timing of gamma activity after movement onset suggests that these oscillations represent either afferent proprioceptive feedback or a relatively late stage of motor control, but probably not early stage motor planning processes. Recent data from Miller et al. (2010) demonstrated that motor cortex primary gamma oscillations can be induced by motor imagery in the absence of both electromyographic and overt movements and, by implication, afferent proprioceptive feedback to the brain. There are several pathways by which proprioceptive information reaches the motor cortex during movement. For example, it is known that muscle spindle afferent pathways project directly from the nucleus ventro-posterior lateralis of the thalamus to the M1 (Lemon and Vanderburg 1979) in addition to their projections to primary somatosensory cortex (Phillips et al. 1971), creating an indirect path to the motor cortex. Regardless of the specific pathway, EEG evidence exists for proprioceptive-related potentials located in the precentral gyrus 90 ms after movement (Seiss et al. 2002). Whether humans can use imagery to activate these proprioceptive pathways is unknown, although the most parsimonious explanation for integrating the current data with previous data (Miller et al. 2010) is that motor cortex gamma oscillations play a role in relatively late stage of motor control rather than proprioception.

In experiment 2 a clear main effect of movement depth was present such that the greater the movement performed, the greater gamma oscillation power observed. The effects on gamma power mapped more closely onto the total amount of movement rather than the peak-to-peak movement size. Of course, this is not to say that displacement itself is necessarily the critical underlying variable of interest. For example, greater movements are also correlated with higher-order parameters.
such as greater onset and peak velocity or acceleration. More detailed experiments will be required to attempt to separate these higher-order behavioral components. Nevertheless, the results are clear that greater movements lead to higher-power gamma oscillations in M1. In contrast, in experiment 3 it could be seen that gamma oscillations were pronounced at the onset of force production but soon dissipated despite the fact that EMG and force production were clearly maintained. This pattern of transient gamma during constant force production is consistent with intracranial data (Crone et al. 1998), which also found that beta power desynchronization was sustained for the entire period of force production. It is worth noting that the onset of force production is nonisometric, given that participants made small initial movements and postural adjustments to generate the initial force, whereas the final 3 s represent a purer isometric contraction. Taken together, the results of experiments 2 and 3 imply that M1 gamma oscillations are more likely to encode kinematic parameters regarding limb movement rather than reflecting the fact that muscles are actively contracting. It has been previously proposed (Mackay 1997) that fast sensorimotor oscillations may be a mechanism for sampling peripheral data to guide subsequent motor acts and the gamma oscillations analyzed here could potentially play a role in such a mechanism. Whether this is indeed the case and how this information is used by the motor system to modulate ongoing motor behavior remains an open question for future investigations.

Experiment 4 tested whether gamma oscillations were dependent on an actual motor signal or whether passive movement would also evoke similar gamma oscillations, via activation of somatosensory systems. The results of this were unequivocal in that there was some 44-fold more gamma in the active over the passive condition, with results being slightly inconsistent as to whether gamma was present at all in the passive movement condition. As such, the gamma oscillations reported here do not appear to be generated by the activity of somatosensory systems during movement.

In summary, the current study has determined a specific set of functional properties of M1 gamma oscillations in response to various movement tasks. Gamma oscillations were found to be stronger for larger movements but were absent during the sustained part of isometric movements, with no finger movement or muscle shortening, and suggests that the information encoded is related to limb movement rather than to muscle contraction. It remains an open question for future investigations to determine the kinematic parameters encoded and how this information modulates ongoing motor behavior.

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